AMENDED VERSION

IN THE SPECIFICATION:

Page 31, line 20 through page 32, lines 1-5:

Transgenic and Knockout Methods: The present invention may provide for transgenic gene and polymorphic gene animal and cellular (cell lines) models as well as for knockout models wherein the gene associated with human female infertility is either inserted and/or the corresponding animal gene "knocked out." These models can, for example, be used for the study of therapeutics for treating infertility. These models are constructed using standard methods known in the art and as set forth in United States Patents 5,487,992, 5,464,764, 5,387,742, 5,360,735, 5,347,075, 5,298,422, 5,288,846, 5,221,778, 5,175,385, 5,175,384, 5,175,383, 4,736,866 as well as Burke and Olson (1991); Capecchi (1989), Davies, et al. (1992), Dickinson et al. (1993), Duff and Lincoln (1995), Huxley et al. (1991), Jakobovits et al. (1993), Pearson and Choi (1993), Rothstein (1991), Schedl et al. (1993), Strauss et al. (1993).

Page 57, lines 5-26:

To determine whether the dysregulated immunoreactive ebaf was the correct immunoreactivity was examined in the endometria of patients with endometriosis. In some women, the endometriosis is associated with infertility whereas in others, its presence does not preclude pregnancy. As compared with the control fertile endometria, the ebaf protein bands were as abundant as those found during the late secretory and menstrual phase (Figure 9, compare with normal control shown in Figure 8). With the exception of one patient, however, this dysregulated expression of the ebaf protein species was more pronounced in infertile women with endometriosis as compared with women with endometriosis who became pregnant (Figure 9). The ebaf immunoreactivity was then examined in the endometria of a 6 infertile women with endometriosis who underwent treatment for their infertility (Figure 10). Four patients, in whom treatment lead to

a decrease in the immunoreactive ebaf bands, subsequently became pregnant after treatment (Figure 10). On the other hand, two additional patients in whom the treatment was associated with an increase in the immunoreactive ebaf bands, did not become pregnant (Figure 10).

Page 58, lines 15 through Page 60, lines 1-5:

DISCUSSION

ebaf was identified as a member of the premenstrual/menstrual molecule repertoire in human endometrium. By Northern blot analysis, the *ebaf* mRNA was abundant in the late secretory and menstrual endometria. Based on the amino acid component of the *ebaf*, the size of the precursor protein was estimated to be 41 kD. Consistent with this size, a 41 kD protein band which appeared as a doublet, when adequately resolved, was detected in the Western blot analysis of the endometrial proteins. The NIH-3T3 cells transfected with *ebaf*, the also expressed the 41 kD protein. Presence of a signal peptide suggested that *ebaf* may be a secreted protein. Three potential cleavage sites exist within the *ebaf* precursor leading to 32.3, 25.7 and 12 kD secreted proteins. The Western blot analysis of endometrium, endometrial fluid, and serum revealed protein bands of 31 and 25 kD. The relatively lower abundance of this protein accounts for the lack of its detection by the Western blot analysis. However, when immunoprecipitated, a ~12 kD protein was also detected in the endometrium. Similarly, the transfection of the NIH-3T3 cells with *ebaf* led to the secretion of a 32 and 25 kD as well as the ~12 kD protein. In addition to these bands, a 55 (55/60) kD protein band was detected by the Western blot analysis in the endometrium, endometrial fluid and serum. Since the immunoreactivity of the antibody with this band could be inhibited by pre-incubation with the peptide, it seems that this band may represent ebaf protein, which in view of its size, may be a post-translationally modified product. Some of the proteins detected in the tissue lysates of endometrium may be secretory products that reside outside the cells and which ultimately enter the peripheral circulation. Consistent with this

hypothesis, the ebaf protein could be detected in the endometrial fluid and sera. The immunohistochemical staining showed that some of the protein is detectable within the endometrial cells. The presence of the 41 kD precursor protein in the serum is unusual. However, the 41 kD was also secreted from the transfected cells indicating that it may be released to the outside of the cells. It is interesting to note that serpins that inhibit Furin and which lack the typical cleavable N-terminal signal sequence have been found to reside extra-cellularly. ebaf protein was found in the male sera indicating that sources other than uterus exist in the body that make *ebaf*. Using Northern blot hybridization, it was shown that the *ebaf* mRNA is expressed, at a low level, in the pancreas, rectum, ovary and testis. The mRNA of many cytokines is expressed at a low copy number, yet, this is sufficient for the translation of an adequate number of cytokine molecules active in the tissue micro environment. This is the basis for the detection of the ebaf protein by Western blot analysis in the endometrium during the proliferative phase of the menstrual cycle, in presence of a low level of *ebaf* mRNA. The 25 kD and not the 31 kD protein bands were detected in the male sera suggesting that only the 31 kD protein may be uterine specific. Thus, the amount of this protein species in the serum reflects the amount of the *ebaf* synthesized by the endometrium.